REMARKS

The Official Action of August 24, 2005, and the prior art relied upon therein have been carefully reviewed. The claims in the application are now claims 1-30, and these claims define patentable subject matter warranting their allowance. The applicant accordingly respectfully requests favorable reconsideration and allowance.

The present application is the U.S. National Phase of PCT/IL02/00890, and claims priority from an earlier application filed in Israel on November 13, 2001. Consistent with international practice, the International Bureau of WIPO will have forwarded a copy of the Israeli priority application to the PTO. Accordingly, as priority has been claimed and the PTO should have a copy of the priority application, **applicant respectfully requests the PTO to acknowledge receipt of applicant's papers filed under Section 119.**

The detailed Action acknowledges receipt of applicant's Information Disclosure Statement. However, the PTO has not provided applicant with an Examiner-initialed copy of the form SB/08a filed as part of such Information Disclosure Statement, whereby applicant will be informed that the Examiner has fully considered citations AA and AB, namely

the Schor and Michelucci U.S. patents mentioned at the top of page two of applicants specification. **Applicant accordingly respectfully requests an Examiner Initialed copy of such form SB/08a.**

As regards the other three references cited by applicant, namely references AC, AD and AE, applicant notes that the Examiner has re-cited these as citations N, O and P, and these are the three references applied in the rejection. Of these, applicant respectfully notes for the record that the Sherman publication, namely WO99/22724, reference O and AD is extensively discussed in applicant's specification at page 3.

Claims 29 and 30 have been added above. Claim 29 is a new independent claim which covers preferred embodiments according to the present invention. New claim 30 depends from claim 29 and specifies the presence of hydroxypropylmethyl-cellulose, contrary to the teachings of Sherman.

Claims 1-28 have been rejected as obvious under Section 103 from Heiligenstein EP' 236 (Heiligenstein) in view of Sherman et al WO' 724 (Sherman) and Jeary et al WO' 099 (Jeary). For the record, there is a corresponding U.S. patent 6,028,070 for Heiligenstein; and a corresponding U.S. patent 6,274,171 and two U.S. patent application publications

2001/055612 and 2002/025339 for Sherman. The rejection is respectfully traversed.

First, the proposed combination would not have been obvious because the references are inconsistent with one another. Thus, to modify Heiligenstein as taught by Sherman and/or Jeary as proposed in the rejection, would have been contrary to Heiligenstein and indeed would have flown in the face of Heiligenstein, the very antithesis of obviousness, for reasons pointed out below.

However, before doing so applicant respectfully notes that the characterization in the rejection of the disclosure of Heiligenstein is incorrect. Heiligenstein does **not** disclose an extended release composition. Contrary to what is stated in the rejection, Heiligenstein discloses and teaches a **delayed** release formulation which has an **enteric coating. The** purpose of the enteric coating is to make sure that the formulation **does not release** formulation in the stomach, i.e. the formulation of Heiligenstein is intended and formulated to **pass through the stomach** protected by the enteric coating. Once the formulation of Heiligenstein has passed through the stomach and into the small intestine, the enteric coating dissolves and the drug is released.

The release mechanism thereof is pH dependent, i.e., the Heiligenstein formulation opens at a pH value above 5.5.

This is an entirely different formulation and mechanism from the extended release formulation of the present invention which provides slow release of the drug over an extended period of time, i.e. about 24 hours. Nothing in the teaching of Heiligenstein would direct a skilled artesian to formulate an extended release formulation.

Jeary discloses and teaches an extended release formulation. The person of ordinary skill in the art seeking to improve the Heiligenstein formulation would never modify Heiligenstein in view of Jeary because the objective in Jeary is totally different than the objective in Heiligenstein. To say the least, there would be absolutely no motive or incentive for taking anything from Jeary, which relates to an extended release composition, for incorporation into Heiligenstein which is directed to a delayed release formulation.

Moreover, even if it were obvious to make such a substitution, respectfully denied by applicant for the reasons pointed out above, the resultant formulation would still not correspond to applicant's claimed subject matter, because the resultant reconstructed Heiligenstein formulation would still be a **delayed release formulation** rather than an extended release formulation.

Returning to the non-obviousness of the proposed combination, the Examiner is correct that Jeary does indeed mention in claim 7 that the Jeary composition may include Venlafaxine. However, there is substantial reason to doubt that such a teaching would be accepted by the person of ordinary skill in the art in view of the focus in Jeary on fluvoxamine which is a **poorly** water soluble drug. How one handles a poorly water soluble drug like fluvoxamine is very different from how one handles a highly water soluble drug like Venlafaxine Hydrochloride, as claimed. Control of time release of a poorly water soluble drug like fluvoxamine, the focus of Jeary, is relatively easy compared with the problem of how to control a highly water soluble drug like Venlafaxine Hydrochloride.

Jeary provides no actual experiments with respect to Venlafaxine. All the examples deal with fluvoxamine, and none deal with applicants claimed Venlafaxine Hydrochloride. In spite of claim 7 of Jeary, the person of ordinary skill in the art with knowledge of the water solubility of Venlafaxine Hydrochloride, would never be guided to abstract anything from Jeary for incorporation into Heiligenstein.

While the rejection includes Sherman as a secondary reference, such a rejection does not explain how Sherman is applicable in the rejection.

Regardless, Sherman is, as mentioned above, discussed at some length in applicant's specification at page 3, where it is pointed out that Sherman's approach is quite different from the claimed approach. Sherman uses the more conventional approach which is mentioned at page 2 of applicant's specification as follows:

> In some cases for example with very water soluble active materials and with relatively high doses it is not feasible to produce tablets which enable appropriate control on the drugs release. This is the case, for example with Venlafaxine Hydrochloride.
>
> In such a case a suitable approach in encapsulating the drug and producing extended release capsules dosage forms. When preparation of such dosage forms is considered, the preferred way is to mix the active ingredients with at least one binding agent to form a uniform mixture which is later moistened with water or with an appropriate organic solvent to form an extrudable plastic mass, from which small particles , cylinders shape (1mm diameter) of drug/matrix are extruded, chopped into appropriate lengths and converted to spheroids using spheronization equipment. These spheroids are further dried and then film coated with an appropriate polymer to form a film with the desired release patterns.

More particularly, applicant's specification states as follows at page 3:

> In WO 99/22724 (AHP, Sherman) a detailed description of preparating an encapsulated dosage form (coated

> spheroids) of Venlafaxine Hydrochloride is provided. By the method described therein, a spheroid core is prepared by extruding and spheronizing a mixture of the drug with microcrystalline cellulose, and then coating it with an ethyl cellulose hydroxypropylcellulose mixture.

The dosage form taught by Sherman is therefore quite different from the dosage form claimed. Applicant does not see how the consideration of Sherman along with Jeary and Heiligenstein could possible have led the person of ordinary skill in the art to applicant's claimed subject matter.

Withdrawal of the rejection is in order and is respectfully requested.

Favorable reconsideration and allowance are earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant

By _____
Sheridan Neimark
Registration No. 20,520

SN:kg
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\M\MAKH\SELA5\PTO\PCTAMD 24JAN06.doc